a3 cancl

Figs. 5A through 5J depict an exemplary web page which conveys to a registered user information about clinical studies, in accordance with the present invention.

Please delete the paragraph on page 13, beginning on line 21 and ending on line 23, and replace it with:

a4 cancl

Figs. 6A through 6R depict a series of exemplary web pages through which a person can search clinical studies and opt to receive information about clinical studies in one or more selected therapeutic areas, in accordance with the present invention.

a5 cancl

Please delete the paragraph on page 14, beginning on line 1 and ending on line 3, and replace it with:

Figs. 7A through 7E depict an exemplary web page that provides a questionnaire that may be completed by an investigator interested in conducting a clinical study, in accordance with the present invention.

Please delete the paragraph page 14, beginning on line 4 and ending on line 5, and replace it with:

a6 cancl

Figs. 7F to 7J depict flow diagrams showing processes for registering subjects and investigators, in accordance with alternative embodiments of the present invention.

Please delete the paragraph on page 14, beginning on line 6 and ending on line 7, and replace it with:

a7 cancl

Figs. 8A and 8B depict a flow diagram showing the steps performed by a sponsor using the professional site to recruit subjects, investigators, arid take steps necessary to start a clinical study.

Please delete the paragraph on page 14, beginning on line 8 and ending on line 9, and replace it with:

a8 cancel.

Figs. 9A and 9B depict an exemplary web page used by a sponsor to enter study parameters into the system.

Please delete the paragraph on page 14, beginning on line 10 and ending on line 11, and replace it with:

a9 cancel.

Figs. 10A and 10B depict an exemplary web page used by a sponsor to enter criteria necessary to initiate an investigator search.

Please delete the paragraph on page 14, beginning on lines 18 and ending on line 19, and replace it with:

a10 cancel.

Figs. 15A through 15H depict an exemplary study-specific subject questionnaire used for prescreening a subject for a clinical study.

Please delete the paragraph on page 15, beginning on line 13 and ending on line 14, and replace it with:

a11 cancel

Figs. 22A through 22K depict an exemplary data structure for implementing an investigator database, in accordance with the present invention.

Please delete the paragraph on page 15, beginning on line 15 and ending on line 16, and replace it with:

a12 cancel

Figs. 22L-P depict use of a disease incidence search on a TIA database to assist in performing investigator and subject selection, in accordance with the present invention.

Please delete the paragraph on page 15, beginning on line 18 and ending on line 19, and replace it with:

a13 cancel

Figs. 24A through 24E depict an exemplary data structure for implementing a subject database, in accordance with the present invention.

Please delete the paragraph on page 15, beginning on line 22 and ending on line 23, and replace it with:

Figs. 26A and 26B depict an exemplary data structure used for implementing the sponsor access limitations shown in Fig. 23.

Please delete the paragraph beginning on page 22, line 13 and ending on page 23, line 10, and replace it with:

Referring still to Figure 1, system 100 also includes an integrated investigator database. In one embodiment, the investigator database includes information from three general sources as described below, although in other embodiments it may include information from a lesser or greater number of sources or different sources. First, the investigator database includes data about the clinical study investigators who wish to inform clinical study sponsors of their clinical study experience and/or training, submitted by the investigators themselves. This self-reported data is typically entered into the investigator database either when a given investigator logs onto the professional site and registers with the system as described further with reference to Figs. 7A through 7E or by submitting such information to the professional site by mail, fax, phone or other non-computerized means. The self-reported data includes various types of information including, for example, the educational background of the investigator, the clinical study experience of the investigator, the past performance of the investigator in other clinical studies (e.g., how many subjects the investigator committed to recruit for a given study and in what period of time, how many subjects the investigator actually recruited for the study and in what period of time, and how many of such subjects actually completed the study), equipment available to the investigator (e.g., whether or not the investigator has access to a CAT scan machine or MRI equipment which may be required for a given study), any mandated IRB

relationships of the investigator (e.g., whether or not the investigator is required through professional affiliations to submit materials to a particular IRB for approval before the materials may be used to advertise the study), any hospital or HMO affiliations of the investigator, information about the investigator's staff and facilities and the geographic location of the investigator.

a15 cont

Please delete the paragraph on page 26, beginning on line 12 and ending on line 21, and replace it with:

Figs. 4A through 4D depict an exemplary web page of subject sites through which a person may submit one or more disease conditions to a database for identifying eligible subjects for a clinical study, in accordance with the present invention. Therapeutic area web page 400 includes pull down menu 401 at which a person may identify a therapeutic area of interest to that person. In this example, the therapeutic area cancer has been chosen. Upon clicking on view button 402, the potential disease conditions of interest are presented to the subject or caregiver in disease condition area 403. The person may check one or more boxes in medical news/drug area 404 or clinical study opportunities area 405 to indicate if the person is interested in obtaining medical news, drug or clinical study opportunity information on any of the disease conditions specified in disease condition area 403.

a16 cont

Please delete the paragraph beginning on page 26, line 22 and ending on page 27, line 4, and replace it with:

Figs. 5A through 5J depict an exemplary web page of the subject site, which conveys information about clinical studies, and provides an ability to search clinical studies to a registered user, in accordance with the present invention. Frequently asked questions area 503 is provided to educate a person on clinical studies. In search area 501, the registered user may

a17 cont

click on any one of the therapeutic areas identified (such as cancer clinical study area 502) and be taken to a search clinical study web page 600, as depicted in Figs. 6A and 6B.

Please delete the paragraph on page 27, beginning on line 12 and ending on line 20, and replace it with:

Upon clicking on contact area 604, the user will be taken to general study interest web page 605 shown in Figs. 6C and 6D. On general study interest web page 605, the registered user may indicate in interest area 606 whether the registered user is interested for himself/herself or for someone else. In one embodiment, the registered user may select in selection area 607 up to three therapeutic areas in which the registered user is interested. In contact area 608, the registered user indicates the manner in which the registered user would like to be contacted, e.g., by e-mail, telephone or regular mail. The registered user also indicates name and contact information in contact information area 609. The registered user submits the form by clicking on submit button 610, or may cancel the process by clicking on cancel button 611.

Please delete the paragraph on page 28, beginning on line 3 and ending on line 16, and replace it with:

In an alternative embodiment, in order to become a user registered with the subject database, the user will be required to provide the information required as shown in the web page depicted in Fig. 6E: a user id; password; password reminder; and whether the user is seeking information for himself or herself or for someone else. In a second step, with reference to Figs. 6F and 6G, the user will be required to provide additional information such as first name, date of birth, gender, electronic mail address, zip code and an indication of one or more medical conditions in which the user is interested. Additional information, though not required for registration, may be provided such as medical conditions experienced by the user, salutation, last

name, ethnic background, telephone number, country of residence, as shown in Fig. 6F. In a third step 3, the user inputs information on a web page such as that shown in Fig. 6H, including a request to receive various types of information (such as, e.g., clinical study opportunities or news and new medical therapies) about the user's medical conditions identified in Figs. 6F and 6G. The user may request that he or she not be sent any information. In area 650, the user is asked to agree to certain terms and conditions governing the user's use of the inventive system.

a19 cancel

Please delete the paragraph beginning on page 28, line 17 and ending on page 29, line 3, and replace it with:

Upon completing the required information and accepting the terms and conditions, the user will become a registered user of the inventive system, as shown in the web page depicted in Fig. 6I. At this point, the user may choose to answer additional, optional questions or to return to the previous activity. If the user chooses to answer additional questions, the riser may be taken to a web pages such as those depicted in Figs. 6J through 6N and provide information such as the type of prescriptions or over-the-counter medications taken by the user for a given medical condition; the health habits of the user; and the clinical study experience of the user. In Fig. 6O, the user can see if the user has answered completely questions about each medical condition previously listed by the user. In Fig. 6P, the user can provide feedback. In Fig. 6Q, the service provider may provide a thank you to indicate that the message was sent successfully.

a20 cancel

Please delete the paragraph on page 29, beginning on line 4 and ending on line 12, and replace it with:

The registered user may also access, on the subject site, the registered user's own personal library. Library web page 612, shown in Fig. 6R, informs the registered user that he or she may maintain a personal library of information relating to clinical studies or new

a21 cont

developments related to particular therapeutic areas found throughout the subject site. The user may also create and save personal notes relating to the same. Information may be placed in the library by the registered user or, in some embodiments, specific information on topics which may be of interest to the registered user may be placed in the registered user's library automatically based on, for example, the registered user's past selections of information to place in the library, therapeutic areas of interest, disease conditions of interest, geographic location, and/or gender.

Please delete the paragraph beginning on page 29 line 14 and ending on page 30, line 6, and replace it with:

An investigator who is interested in conducting clinical studies may express his or her interest by registering on the professional site of Fig. 1B. Figs. 7A, 7B, 7C, 7D, and 7E depict investigator questionnaire web page 700 that provides a questionnaire that may be completed by an investigator interested in conducting a clinical study, in accordance with an embodiment of the present invention. In name area 701, the investigator is required to input his or her name. In degree area 702, the investigator's degree(s) are required. The PRF organization or institutional name, address, city state, country, zip code and telephone number are required (and fax and electronic snail address optionally requested) in contact area 703. Specialty area 704 requires that the investigator provide his or her primary specialty area. Board area 705 requires that the investigator indicate whether he or she is board certified and/or board eligible; optionally, the investigator's year of primary specialty board certification, and board information regarding any of the investigator's subspecialties may be provided. In study experience area 706, the investigator is required to indicate the number of years the investigator has participated in clinical studies as well as all phases of clinical research in which the investigator has

a22 cont.

participated. The investigator must include the number of investigators that conduct research at the PRF indicated in investigator area 707.

Please delete the paragraph on page 31, beginning on line 2 and ending on line 9, and replace it with:

a23 cont.

Figs. 7F to 7G depict flow diagrams showing processes for registering subjects and investigators, in accordance with alternative embodiments of the present invention. Fig. 7F is directed to persons that register with the subject or investigator site based on a visit to the subject site; Fig. 7G is directed to persons that register with the subject or investigator site based on a contact with a pharmaceutical call center; Figs. 7H and 7J are directed to persons that register with the subject or investigator site based on a contact with an off-line call center and Fig. 7J is directed to persons that register with the subject or investigator site based on a visit to a third party on-line recruitment site.

Please delete the paragraph on page 31, beginning on line 11 and ending on line 15, and replace it with:

a24 cont.

Referring now to Figures 8A and 8B, there is shown a flow diagram of a process that may be used by a sponsor to accomplish the steps necessary to start a clinical study. The process may begin at two different points. Specifically, if the sponsor wishes to begin by making a feasibility assessment with respect to the study, the process starts at step 804. Alternatively, if the sponsor does not wish to make a feasibility assessment, the process starts at step 811.

Please delete the paragraph beginning on Page 33, line 15 and ending on page 34, line 8, and replace it with:

a25 cont.

The sponsor reaches step 811 either as an entry point into the process, or after the sponsor has determined in step 810 that the study is feasible. In step 811, tile sponsor determines

whether the sponsor desires to use the investigator database to perform investigator recruitment for the study. If the sponsor wishes to use the investigator database for investigator recruitment, then in step 815, the sponsor begins by entering study parameter information into the system. A screen shot of a web page that may be used for entering this information is shown in Figures 9A and 9B. In this step, the sponsor enters various parameters about the study into the system. Next, in step 816, the sponsor enters investigator search criteria for the study into the system. Such search criteria could include, for example, one or more specialties that would be desirable for an investigator for the study, information about the prescribing behavior of the investigator, the number of studies that the investigator has conducted, the therapeutic area and disease indication associated with clinical studies previously conducted by the investigator, the distance around the investigator site in which subjects participating in the study should be sought, and the geographic area in which the investigator should be located. Figures 10A and 10B depict a screen shot of an exemplary web page that may be used by a sponsor to input the investigator search criteria into the system. In step 818, the sponsor is given the ability to weigh one or more of the investigator criteria prior to initiating the investigator search.

Please delete the paragraph beginning on Page 34, line 18 and ending on page 35, line 8, and replace it with:

An exemplary web page that shows the results of an investigator search in accordance with the present invention is shown in Figs. 11A and 11B. As shown in that figure, for each investigator identified in the search, the sponsor is shown the name of the investigator, the investigator's specialty, the city/state in which the investigator is located, the number of studies that the investigator has performed, subject demographic information obtained from the TIA database (i.e. the number of persons listed in the TIA database that are within a predetermined

distance of the investigator site and who could potentially qualify as subjects for the clinical study), subject demographic information obtained from the subject database (i.e. the number of subjects listed in the subject database that are within a predetermined distance of the investigator site and who could potentially qualify to participate in the clinical study), the drug prescribing behavior of the investigator (e.g., the drug class prescribing decile associated with the investigator). It will be understood by those skilled in the art that other criteria relevant to the investigator could also be shown on this search results screen including for example, the behavior of the investigator with respect to ordering of laboratory tests/procedures.

Please delete the paragraph beginning on Page 36, line 22 and ending on page 37, line 19, and replace it with:

After a potential subject has been identifies (step 817 or 819), the process of pre-screening for participation in the study begins (step 824). In this step, subjects identifies using on-line and/or offline recruitment are notified, and asked whether or not they have an interest in participating in the clinical study. In the case of candidates that were identified on-line using the subject database, the subjects are preferably contacted by the means that they identified during their registration, on the subject site (e.g., by electronic mail) in order to preliminarily determine whether they have an interest in participating in the clinical study. A screen shot of an exemplary e-mail used for providing such a notification to a potential subject is shown in Fig. 14. The notification could alternatively be provided using telephone, mail, fax or any off line communication means. If a potential subject responds to a notification by indicating interest in participating in a clinical study, the subject is provided with a formal questionnaire that asks for information specifically relevant to the clinical study. An exemplary study-specific subject questionnaire is shown in reference to Figs. 15A-15H. In the preferred embodiment, if in

response to the e-mail notification shown in Fig. 14, the subject indicates interest in participating in the clinical study, a study-specific subject questionnaire such as shown in Figs. 15A-15H is provided to the subject on a secure web page found on the subject site. The subject then uses this secure web page to answer all of the questions in the subject questionnaire, and to submit such answers for consideration. As mentioned above, irrespective of whether the subject is ultimately selected for participation in the clinical study, these questionnaire answers are stored in the subject database with the consent of the patient, thereby enriching the subject information stored in that database.

Please delete the paragraph on page 39, beginning on line 2 and ending on 7, and replace it with:

Fig. 16 is a process flow diagram of a method for identifying eligible investigators for a clinical study in accordance with one embodiment of the present invention. Specifically, at step 1610, information is stored in database 2200 of the inventive system (in particular, the data is stored in table 2252, field 2252a of Fig. 22E) relating to the geographic location of each of a plurality of investigators. At step 1620, an incidence or a prevalence of each of a plurality of disease conditions in a plurality of different geographic locations is stored in the database.

Please delete the paragraph on page 46, beginning on line 13 and ending on line 18, and replace it with:

At step 2141, information is stored in the database that associates the types of equipment that an investigator has with one or more disease condition. At step 2142, the database is queried wherein information representing a selected disease condition associated with the specific clinical study is used. The query will result in correspondence between the specific disease

condition and related equipment that an investigator has. At step 2143 the inventive system identifies an investigator based upon the query results and the investigator's equipment.

Please delete the paragraph beginning on Page 46, line 19 and ending on page 47, line 2, and replace it with:

Fig. 21L is a process flow diagram depicting the steps of a method for identifying eligible investigators for a clinical study in accordance with yet a further embodiment of the present invention. At step 2143', information is stored in the inventive system database relating to prospective investigators for clinical studies, which includes the investigator practice setting, which is where the actual clinical study is conducted, and where a subject would most likely go to participate. 'this information is provided by the investigator.

Please delete the paragraph beginning on Page 59, line 15 and ending on page 60 line 2, and replace it with:

Fig. 22A through 22K is an exemplary data structure for implementing an investigator database 2200. For example, table 2210 includes investigator data related to basics such as name, age, address, phone, etc. Table 2220 contains data about a specific study performed by the investigator, Table 2230 relates to the investigator's specialties, and Table 2240 relates to the investigator's subject population. Shown in Figs. 22C and 22E, table 2250 contains data about the investigator's staff. Table 2260 of Fig. 22F contains data regarding the investigator's hospital affiliations. It will be understood by those skilled in the art that the investigator database of the present invention could be implemented using many different formats or structures, and that the particular structure shown in Figs. 22A thorough 22K represents one example of such a data structure.

Please delete the paragraph on page 60, beginning on line 4 and ending on line 20, and replace it with:

Figs. 22L-P depict use of a disease incidence search on a TIA database to assist in performing investigator and subject selection. The example shown relates specifically to use of the invention to perform a study related to the disease of angina. Initially, the TlA database is queried using angina as the query criterion to identify geographic locations where the incidence of angina is more prevalent. These areas are identified on a national basis in Fig. 22L, and specifically for the Dallas-Fort Worth area in Fig. 22M. It bears noting that, within the Dallas-Fort Worth area, the TlA database IMS further identified an incidence value for each sub-region of the Dallas-Fort Worth area. Sites of various investigators in Dallas-Fort Worth that are potentially eligible to perform the study are also shown on Fig. 22M. These investigator sites were found by querying the investigator database as described above. Fig. 22N shows that there are three eligible investigator sites in the Dallas-Fort Worth Area. These three investigator sites are shown as circled stars in Fig. 22N. Of the three eligible investigator sites, one of the investigator sites is located in a sub-region having a higher incidence of angina than is found in the sub-regions of the other two eligible investigators. As shown in Fig. 22O, the investigator located in the sub-region having the highest incidence of angina is next selected to perform the study. Following selection of this investigator for the study, subjects closest to the site of the selected investigator are identified for screening, as shown in Fig. 22P.

Please delete the paragraph on page 61, beginning on line 12 and ending on line 15, and replace it with:

Fig. 23 is a screen shot showing sponsor access limitations to study data. Aggregated data 2302 can be viewed by all sponsors, whereas data 2304 can only be viewed by the sponsor that